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Rotavirus gastroenteritis among children less than 5 years of age in private outpatient setting in urban India☆

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ABSTRACT

Burden of rotavirus gastroenteritis (RVGE) in outpatient setting in India is not fully understood. A prospective study was undertaken to describe RVGE among Indian children less than 5 years of age presenting in outpatient departments with acute gastroenteritis (AGE). This study was conducted at 11 outpatient departments (OPDs) of private pediatric clinics in urban areas of India. A total of 605 eligible children were enrolled at OPDs. Stool samples of the subjects were collected and tested for presence of rotavirus antigen by enzyme immune assay (EIA) and were typed by reverse-transcriptase polymerase chain reaction (RT-PCR). Physician examined the children and documented the disease particulars. In addition, parents/guardians were interviewed for AGE related symptoms, health care utilization and cost incurred due to AGE, and parental stress associated with AGE. After OPD, parents/guardians completed diary cards and questionnaires to capture the information for 14 days following the enrollment.

Complete data for analysis including stool sample results was available from 552 subjects. 23% (127/552; [CI 19.5, 26.5]) of stool samples were rotavirus (RV) positive. RT-PCR was done for 85.8% (109/127) of RV positive samples. G1, G2, G9, and G12 types were identified in 34.9% (38/109), 37.6% (41/109), 8.3% (9/109), and 6.4% (7/109) stool samples, respectively. P[4] and P[8] were identified in 36.7% (40/109) stool samples each, followed by P[6] identified in 15.6% (17/109) stool samples.

At the time of enrollment, all three symptoms (vomiting, diarrhea, and fever) were observed concurrently in higher proportion of RV positive subjects compared to RV negative subjects (60.6% [77/127] vs. 42.8% [182/425], $p = 0.0004$). Healthcare resource utilization, costs incurred due to disease, and parental stress were higher for RV positive subjects compared to RV negative subjects.

In conclusion, RVGE was found to be a definite burden in AGE cases attending pediatric outpatient clinics in urban areas and it was associated with substantial economic and psychological burden. Introduction of rotavirus vaccine in India may help in reducing this disease burden.

1. Introduction

The burden of diarrhea caused by rotavirus infection in the pediatric population is a major cause of concern worldwide. It is estimated that in 2008, rotavirus diarrhea or rotavirus gastroenteritis (RVGE) resulted in 453,000 deaths worldwide in children aged less than 5 years, which accounted for 5% of all deaths in this age group [1]. This estimate is after excluding the post vaccine

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introduction data if any. India alone accounted for approximately 22% of world RVGE deaths (98,621 deaths) in children aged less than 5 years [1]. These figures clearly indicate high burden of rotavirus mortality among Indian children. Rotavirus associated morbidity in India is also well documented. Many Indian studies including the Indian Rotavirus Strain Surveillance Network (IRSN) have evaluated RVGE burden amongst hospitalized cases of acute gastroenteritis (AGE) and some studies also demonstrated rotaviruses strain diversity as in other developing countries [2–6]. These hospital based studies included testing stool samples for rotavirus and to determine the causative rotavirus strains. However, well designed study data is not available with respect to burden of RVGE as well as causative rotavirus strains when AGE cases are enrolled in pediatric outpatient settings and are followed up for the disease spectrum. We conducted an observational study to understand the epidemiological profile of RVGE in private outpatient settings in India. Earlier reports of studies conducted in hospitalized settings probably represent severe cases of RVGE that needed hospitalization, while the present study aimed to include information on disease caused by RVGE which is seen first in the outpatient department (OPD). The objective of the study was to describe RVGE in children aged less than 5 years who attended OPDs of private pediatric clinics in urban areas. Accordingly stool samples of AGE subjects were tested to determine rotavirus positivity and RV positive samples were tested for G and P types. Other characteristics of RVGE like clinical presentation, severity, economical and psychological impact on the parents/family of the children were also studied and compared to non-RVGE.

2. Materials and methods

2.1. Study design

This was an observational, prospective study conducted at 11 sites located in urban areas across all five geographical (north, south, east, west, and central) regions of the country. Children less than 5 years of age who attended the OPD of private pediatric clinics for the treatment of AGE were enrolled. The study was conducted over a period of 11 months (15 December 2011–14 November 2012); however individual sites differed in their study duration due to variation in AGE burden and monthly enrollment rate.

2.2. Study population

Parents/guardians of children aged less than 5 years (60 months) who suffered from AGE and attended OPD, were informed about the study in detail. Children who met the eligibility criteria were included in the study after written informed consent obtained from the parents/guardians. AGE was defined as three or more loose or watery stools and/or one or more episodes of forceful vomiting in a 24-h period. These symptoms must have occurred within 3 days prior to the OPD visit. Children who were enrolled in any other trial, or had history of rotavirus infection, or had received a rotavirus vaccine were excluded. Children with any such condition that in the opinion of the investigator could interfere with the study objectives were excluded. Children whose parents were unable to give consent were also excluded.

2.3. Data collection

After receiving written informed consent, the following information was gathered from the parent/guardian using questionnaire: subject's demographics including medical history, socio-economic details (e.g. annual family income, area of residence), and family details (e.g. number of members in family, number of siblings); information about direct costs (e.g. OPD, medicines, extra drinking fluids, expenses on conveyance for visit), and impact caused by RVGE (e.g. monetary impact of lost days of work for parent/guardian and parental stress). The monetary impact of lost days of work was calculated based on daily wages of the parent/guardian. The stress suffered by the parent/guardian due to child's disease was scored on a scale of 0–10, where '0' was no stress and '10' was extreme stress.

At enrollment, following detailed clinical data were recorded using questionnaire: date of onset of symptoms (diarrhea, vomiting, and fever), number of days for which each symptom continued, maximum frequency of stools and vomiting episodes per day, maximum temperature recorded, dehydration status, behavioral signs and symptoms, and treatment given to the subject. The severity of dehydration of the subject was assessed as mild, moderate, or severe by the investigator based on patient examination for restlessness, lethargy, sunken eyes, skin pinch, normal or poor feeding. The number of IV rehydration bottles administered to the subject was also recorded. Occurrences of behavioral signs and symptoms such as irritable/less playful, lethargic/listless, and convulsions were also recorded. The parent/guardian was given a diary card and questionnaires to record follow-up information on daily symptoms of the subject, and costs and impact caused due to the disease. The questionnaire used on the day of enrollment and follow-up questionnaires used to collect information after OPD visit or Day 1 were designed specifically for this study, and contained simple and easily understandable questions in local vernacular language. The parent/guardian was trained to fill the diary card and questionnaires.

Study personnel made two telephonic contacts with the parent/guardian, first after Day 7 and second after Day 14, for collecting follow-up information for Day 1–Day 7 and Day 8–Day 14, respectively. Additional information such as healthcare utilization (e.g. repeat OPD visit/s, hospitalization, intravenous [IV] hydration) and impact of disease and its progress during Day 1–Day 7 and Day 8–Day 14 was also collected telephonically.

2.4. Assessment of severity

The severity of AGE was scored by the physician based on physical examination of child and the information collected for the duration and severity of disease symptoms. Two scales, namely: Clark scale and Vesikari scale which have been used earlier in clinical trials on rotavirus vaccines were used. The Clark scale is a 24-point scale based on duration and frequency of diarrhea and vomiting, degree and duration of fever measured by rectal temperature, and description and duration of behavioral symptoms. Axillary temperature measurements were used instead of rectal measurements. Conversion of axillary temperature to rectal temperature was performed using following formula [7]: rectal temperature (°C) = 0.98 × axillary temperature (°C) + 0.8 (°C).

The Clark scale is divided into three ranges: mild <9, moderate 9–16, and severe >16.

The Vesikari scale is a 20-point scale based on duration and peak frequency of diarrhea and vomiting, degree of temperature, severity of dehydration, and treatment provided to the patient (i.e., rehydration or hospitalization). This scale is divided into three ranges: mild <7, moderate 7–10, and severe ≥11 [8,9].

2.5. Stool sample collection and laboratory analysis

Stool sample (1.5–5 g) was collected for each subject, preferably at enrollment, or later but within 14 days of the onset of AGE symptoms. The stool samples were stored at 2–8 °C. Samples were shipped to The Wellcome Trust Research Laboratory (Department of Gastrointestinal Sciences, Christian Medical College, Vellore, Tamil Nadu), which was the central laboratory for